

Evidence-Based Emergency Medicine

Clinical Synopsis

TAKE HOME MESSAGE

In patients with non-ST-segment elevation acute coronary syndromes who do not undergo early percutaneous coronary intervention, administration of platelet glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors, given in addition to aspirin and unfractionated heparin, does not reduce 30-day or 6-month mortality. For the composite endpoint of myocardial infarction or death, there was modest benefit at 30 days and 6 months; however, there was an increased risk of major hemorrhage among those receiving GPIIb/IIIa inhibitors.

METHODS

DATA SOURCES

Searches were conducted of MEDLINE (1966 to 2006), EMBASE (1980 to April 2006), and the Cochrane's CENTRAL register (Issue 2, 2006), and hand-searched information from cardiology conferences, principal investigators of identified trials, pharmaceutical manufacturers, and other experts in the field were used. There were no language restrictions.

STUDY SELECTION

Randomized controlled trials enrolling patients with non-ST-segment elevation acute coronary syndromes who initially received GPIIb/IIIa inhibitors as part of the early medical management were eligible.

An installment of the Systematic Review Abstract series:

Update: Use of Platelet Glycoprotein IIb/IIIa Inhibitors in Patients With Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction

EBEM Commentator

Maude Latulippe, MD, CCFP-EM

Eddy S. Lang, MD, MDCM, CCFP-EM

University of Calgary, Faculty of Medicine, Division of Emergency Medicine Foothills Medical Centre, Calgary, Alberta, Canada

Commentary

In patients with non-ST-segment elevation acute coronary syndromes treated with concomitant aspirin and unfractionated heparin who are not immediately referred for percutaneous coronary intervention, GPIIb/IIIa inhibitors do not reduce mortality and only modestly reduce the risk of nonfatal myocardial infarction at 30 days and at 6 months. This benefit comes at the expense of a small increased risk of major bleeding.

The eligibility criteria for most of these studies consisted of the presence of ST-segment changes or positive biological markers of myocardial injury, both features that are known to select high-risk patients.

Yet despite this, the well-powered findings of this review were not significant for mortality reduction.

According to the modest reduction in the composite endpoint (death or myocardial infarction), balanced by the increased risk in major bleeding, there is little support for the routine use of GPIIb/IIIa agents in patients not scheduled for early percutaneous coronary intervention (usually <48 hours). Given the cost and resource considerations related to administration of these medications, more easily administered oral clopidogrel may be a better treatment option in the emergency department setting.^{1,2}

Recent studies have suggested a mortality reduction for the concomitant

DATA EXTRACTION AND SYNTHESIS

Primary outcomes were 30-day and 6-month mortality and the subsequent development of myocardial infarction; the secondary endpoint was major hemorrhage, defined as intracranial bleeding or any bleeding with a decrease in hemoglobin of greater than 5 g/dL or a greater than 15% reduction in hematocrit level. Data were reported as odds ratios (ORs) with a fixed-effect model if minimal heterogeneity was identified; otherwise, a random-effects model was used. All analyses were presented as intention to treat.

use of clopidogrel and GPIIb/IIIa agents in high-risk patients.³ However, those patients are mostly also managed with percutaneous coronary intervention. GPIIb/IIIa inhibitors and clopidogrel have never been compared directly in a prospective head-to-head study in patients with non-ST-segment elevation acute coronary syndromes.⁴

RESULTS

Eight studies involving 30,351 patients used GPIIb/IIIa as the initial medical treatment for patients with non-ST-segment elevation acute coronary syndromes. When the risk of bias was analyzed by the 3 authors, all 8 studies were rated as adequate for allocation concealment. Four GPIIb/IIIa inhibitors, abciximab (1 trial), eptifibatid (2 trials), tirofiban (2 trials), and lamifiban (3 trials), were used. Data from 8 trials provided 1-month mortality, subsequent myocardial infarction rates, and risk of major hemorrhage, whereas data from only 3 trials (45% of patients included in the

Outcomes for patients presenting with non-ST-segment elevation acute coronary syndromes treated with GPIIb/IIIa as the initial treatment compared with standard treatment.

| Intervention | OR (95% Confidence Interval) | | | | |
|---|------------------------------|---------------------------------------|---------------------|--|-----------------------|
| | 30-Day Mortality | 30-Day Death or Myocardial Infarction | 6-Month Mortality | 6-Month Death or Myocardial Infarction | 30-Day Major Bleeding |
| As initial medical treatment of non-ST-segment elevation acute coronary syndromes | 0.92 (0.81–1.04) | 0.92 (0.86–0.99) | 1.01 (0.88–1.16) | 0.88 (0.81–0.96) | 1.27 (1.12–1.44) |

overall review) provided 6-month mortality or myocardial infarction rates.

1. Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators (CURE). Effects of clopidogrel in addition to aspirin patients with acute coronary syndromes without ST segment elevation. *N Engl J Med*. 2001; 345:494-502.
2. Mehta RH, Roe MT, Chen AY, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet*. 2001;358:527-533.
3. Kastrati A, Mehilli J, Neumann FJ, et al. Abciximab in patients with acute coronary syndromes undergoing percutaneous coronary intervention after clopidogrel pretreatment. The ISAR-REACT 2 Randomized Trial. *JAMA*. 2006;295:1531-1532.
4. Pollack CV Jr, Braunwald E. 2007 Update to the ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: implications for emergency department practice. *Ann Emerg Med*. 2008;51: 591-606.

This is an update of a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area. The source for this systematic review abstract is: Bosch X, Loma-Osorio P, Murrugat J. Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes. *Cochrane Database Syst Rev*. 2009;(1):CD002130. DOI: 10.1002/14651858. CD002130. The *Annals'* EBEM editors

helped prepare the abstract of this Cochrane systematic review.

Systematic Review Author Contact

Xavier Bosch, MD, PhD
Cardology Department
University of Barcelona
Hospital Clinic Villarroel
Barcelona, Spain
E-mail: xbosch@clinic.ub.es